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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/019,049	03/28/2002	Jorg Rosenberg	0480/01221	5165

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EXAMINER	
FUBARA, BLESSING M	

ART UNIT	PAPER NUMBER
1618	

DATE MAILED: 03/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/019,049	ROSENBERG, JORG ET AL.	
	Examiner	Art Unit	
	Blessing M. Fubara	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 December 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Examiner acknowledges receipt of amendment and remarks filed 12/06/05. Claims 1 and 3-19 are pending.

Claim Rejections - 35 USC § 112

1. The rejection of claims 5 and 6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the amendment.

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claim 18 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification as originally filed does not describe a paroxetine formulation that is free of volatile organic solvent. Substantially free is not "free." Therefore, claim 18 recites new mater that does not exist in the specification as originally filed.

Claim Rejections - 35 USC § 102

4. Claims 1, 3 and 14-17 remain rejected under 35 U.S.C. 102(b) as being anticipated by the 1998 PDR, pages 2851-2856.

Applicants argue that the PDR discloses a film coated tablet and the hydropromellose film does not contain ant paroxetine.

5. Applicants' arguments filed 12/06.05 have been fully considered but they are not persuasive. Pages 2851-2856 of the 1998 PDR were provided to applicants. On page 2851, column 1, last 5 –6 lines and column 2, lines 1-3, it is stated that inactive ingredients are ... and does not state that the hydropromellose is the film coat and does not contain the active paroxetine. The rejection follows below.

The 1998 PDR in the relevant pages discloses a dosage form of paroxetine-HCl, the dosage form is a tablet and the each tablet contains paroxetine hydrochloride, dibasic calcium phosphate dehydrate, hydroxypropylmethylcellulose, polyethylene glycols, polysobate 80, sodium starch glycolate, titanium diode and one or more colors. The glass transition temperature recited for the polymer is a property of the polymer that cannot be separated from the polymer. It is noted that no specific polymer is recited and thus any synthetic polymer would meet those limitations. Therefore, the PDR reference meets the limitations of the claims.

6. Claims 1-3, 9, 10 and 13-17 remain rejected under 35 U.S.C. 102(a) as being anticipated by Krape et al. (WO 99/00131, provided by applicants on Form PTO-1449). New claim 19 is included in the rejection. Therefore, claims 1-3, 9, 10, 13-17 and 19 remain rejected under 35 U.S.C. 102(a) as being anticipated by Krape et al. (WO 99/00131, provided by applicants on Form PTO-1449).

Applicants argue that the WO publication to Krape's disclosed paroxetine formulation is not substantially free of volatile organic solvent and that Krape defines substantially free as having less than 20% by weight of residual non-aqueous solvent, preferably less than 10%m

more preferably less than 5% and most preferably less than 1% and that this definition is dissimilar to the definition provided by the instant preparation. Applicants state that a definition of substantially free is provide by the prior art and the instant specification.

7. Applicants' arguments filed 12/06/05 have been fully considered but they are not persuasive.

Although applicants state that the instant specification provides a definition for substantially free of volatile solvent, applicants do not provide the page number and the lines on the page where the definition is provided. Secondly, as per applicants' admission, Krape's most preferred level of substantially free is less than 1% and it is Examiner's position that less than 1% is substantially free absent applicants' definition of what applicants mean by substantially free. It is also noted that substantially free is relative and absent applicants specific definition, less that 5% is also substantially free as substantially free may be differ according to who is defining it. Thus, Krape's Example 4 where a 4% volatile organic solvent is detected is substantially free of organic solvent. It is further noted that applicants have not claimed ---free of volatile organic solvent---; the reference to new claim 18 is noted and new claim 19 is included in this rejection because Krape's formulation contains polyvinylpyrrolidone. New claim 18 contains new matter as the specification as originally filed does not state free of volatile organic solvent. Substantially free of organic solvent is not the same as free of volatile organic solvent. The rejection follows below.

Krape discloses solid dispersion of paroxetine in polyvinylpyrrolidone or polyethylene glycol polymeric carrier (abstract, page 5, lines 31-34). In a preferred embodiment, Krape discloses a process for forming the paroxetine-HCl polymer melt that involves heating a mixture

of the paroxetine and polymer carrier to form a molten homogenous melt of paroxetine free base and the polymeric carrier and introducing dry hydrogen chloride into the vessel where a pharmaceutically acceptable paroxetine-HCl is formed in the molten state (page 6, line 27 to page 7 line 7). In example 1, Krape forms a homogenous melt of paroxetine free-base and PEG in a flask and subsequently scraps the product from the flask to grind or mill into desired particle size. Granules of claim 16 read on particles.

The claimed invention is directed to a solid or semisolid preparation of paroxetine or one of its physiologically acceptable salt in the form of a molecular dispersion of paroxetine in a pharmaceutically acceptable polymer matrix having a glass transition temperature of >90 °C. The instant specification on page 1, lines 36-41, describes dispersions of two or more solids as solid solutions or molecular dispersions. The melt of paroxetine and polymer carrier in Krape is a solid solution or molecular dispersion of paroxetine in a polymer. No specific polymer is claimed in the instant invention. The glass transition temperature of a polymer is specific to a specific polymer. Thus the recited glass transition temperature of >90 °C is inherent to the polymeric carrier of the prior art. Paroxetine-HCl is formed when dry hydrochloric acid is introduced into the homogenous melt of the polymeric carrier and paroxetine free-base and this teaching meets the limitation of claim 2. In instant claim 3, 80% of the active ingredient is released after 30 minutes and this property is inherent to the paroxetine formulation of Krape. Regarding the limitation of substantially free of volatile organic solvent, it is noted that substantially free is not free of the organic solvents. A 4% volatile organic solvent detected in Example 5 of Krape would mean substantially free. There is no standard given or recited to define how much residual volatile organic solvent left in the product would constitute

substantially free. Krape in page 13, lines 10 to 29 anticipates evaporating the solvent under vacuum, rotoevapoation, static vacuum drying and combinations and specifically states that the preparation is substantially free of solvents and in these lines defines what the prior art considers to be substantially free of non-aqueous solvent. Thus, the teaching of Krape anticipates the claims.

Claim Rejections - 35 USC § 103

8. Claims 4-8 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Krape et al. (WO 99/00131, provided by applicants on Form PTO-1449) in view of Remon et al. ("Extrusion-spheronisation: A literature Review,'' International Journal of Pharmaceutics, 116 (1995) pp 131-146).

Applicants argue that Remon's wet extrusion cannot be combined with the melt extrusion method of Krape.

9. Applicants' arguments filed 12/06/05 have been fully considered but they are not persuasive.

Remon is relied upon for a teaching that the most popular method of forming pellet from a melt is extrusion. The motivation from the teaching of Remon is the expectation of forming pellets. The rejection follows.

The teaching of Krape is discussed above. Claim 6, which is dependent on claim 5, is taught in Krape because Krape employs paroxetine free-base in the formation of molten homogenous melt of paroxetine-HCl and polymer. Although Krape discloses forming a homogenous melt of paroxetine-HCl and polymeric carrier and optionally grinding or milling the

melt to desirable particles (example 1 of Krape), Krape's melt was formed in a flask and not in an extruder. Thus regarding claim 4, Krape does not teach forming the melt in an extruder. However, it is known to form and shape melts in extruder. For example, the review article by Remon et al., discloses that the most popular method of forming pellets from a melt is by extrusion (see page 132, left column and first full paragraph; and page 134, left column and first paragraph).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare the paroxetine-HCl polymer melt according to Krape. One having ordinary skill in the art would have been motivated to perform the melt and shaping process in an extruder according to what is known in the art with the expectation of producing directly tabletable particles or granules.

10. Claims 11 and 12 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Krape et al. (WO 99/00131) in view of Miranda et al. (US 5,656,286).

Applicants state that claim 1 is patentable "in light of the cited art" and the claims dependent of the claim 1 are accordingly patentable.

11. Applicants' arguments filed 12/06/05 have been fully considered but they are not persuasive.

12. Regarding claims 11 and 12, applicant's arguments fail to comply with 37 CFR 1.111(b) because they amount to a general allegation that the claims define a patentable invention without specifically pointing out how the language of the claims patentably distinguishes them from the references.

13. Regarding claims 11 and 12, applicant's arguments do not comply with 37 CFR 1.111(c) because they do not clearly point out the patentable novelty which he or she thinks the claims present in view of the state of the art disclosed by the references cited or the objections made. Further, they do not show how the unamended claims avoid such references or objections. The rejection below follows.

Krape is described above. Krape discloses paroxetine-HCl PEG melt. Krape does not disclose forming the melt with copovidone polymer. However, Miranda discloses composition comprising paroxetine and copovidone, a copolymer vinyl acetate and vinylpyrrolidone (abstract; column 2, lines 51-57; column 6, lines 26-34; column 2, line 64 to column 3, line 1; column 3, lines 2-7; column 18, line 16; also see Buhler et al., US 6,592,900, column 1, lines 13 and 14 as a teaching reference for Vinylpyrrolidone/vinyl acetate copolymer as copovidone). Miranda is thus relied upon for a teaching of paroxetine and copovidone. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare the paroxetine-HCl polymer melt according to Krape. One having ordinary skill in the art would have been motivated to substitute the polymer of Mirander for PEG with the expectation of forming a melt of the paroxetine.

No claim is allowed.

14. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Blessing M. Fubara whose telephone number is (571) 272-0594. The examiner can normally be reached on 7 a.m. to 3:30 p.m. (Monday to Friday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER